

=> fil medlin embas biosis drugu uspatall
FILE 'MEDLINE' ENTERED AT 16:08:03 ON 25 JUN 2004

FILE 'EMBASE' ENTERED AT 16:08:03 ON 25 JUN 2004
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CA INDEXING COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'USPAT2' ENTERED AT 16:08:03 ON 25 JUN 2004
CA INDEXING COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY (ACS)

=> s (l5 or l13) and bipol?
L22 9 (L5 OR L13) AND BIPOL?

=> dup rem l22
PROCESSING COMPLETED FOR L22
(L23 7 DUP REM L22 (2 DUPLICATES REMOVED)
ANSWER '1' FROM FILE MEDLINE
ANSWERS '2-7' FROM FILE USPATFULL

=> d l23 bib ab 1-7

L23 ANSWER 1 OF 7 MEDLINE on STN DUPLICATE 1
AN 2004043865 MEDLINE
DN PubMed ID: 14744468
TI Ethanolamine and phosphoethanolamine inhibit mitochondrial function in vitro: implications for mitochondrial dysfunction hypothesis in depression and **bipolar** disorder.
AU Modica-Napolitano Josephine S; Renshaw Perry F
CS Department of Biology, Merrimack College, 315 Turnpike Street, North Andover, MA 01845, USA.
NC MH 8681 (NIMH)
SO Biological psychiatry, (2004 Feb 1) 55 (3) 273-7.
Journal code: 0213264. ISSN: 0006-3223.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200404
ED Entered STN: 20040128
Last Updated on STN: 20040402
Entered Medline: 20040401
AB BACKGROUND: A growing body of experimental evidence suggests that mitochondrial dysfunction, including alterations in phospholipid metabolism, might be involved in the pathophysiology of affective illnesses, such as depression and **bipolar** disorder. The purpose of this study was to determine whether the phosphomonoester phosphoethanolamine (PE) and the lipid metabolite choline (Cho), which are known to be altered in depression and **bipolar** disorder, and/or

their precursors/metabolites, might directly affect mitochondrial bioenergetic function in vitro. METHODS: To this end, rates of oxygen consumption in freshly isolated, intact mitochondria were determined polarographically in the presence and absence of PE, Cho, ethanolamine (Etn), glycerophosphoethanolamine (GPE), and glycerophosphocholine (GPC). RESULTS: The data demonstrate that PE and Etn inhibit mitochondrial respiratory activity in a dose-dependent manner, whereas Cho, GPC, and GPE have no measurable effect on bioenergetic function. CONCLUSIONS: This reflects a specific inhibition by Etn and PE on mitochondrial function rather than a more generalized phenomenon induced by similarities in structure between the lipid metabolites. These results also suggest a possible relationship between mitochondrial dysfunction and altered phospholipid metabolism in the brains of patients with depression and **bipolar** disorder.

L23 ANSWER 2 OF 7 USPATFULL on STN

AN 2004:44994 USPATFULL

TI Phospholipid derivatives of valproic acid and mixtures thereof

IN Kozak, Alexander, Rehovot, ISRAEL

PI US 2004033987 A1 20040219

AI US 2003-312895 A1 20030711 (10)

WO 2001-IL629 20010710

DT Utility

FS APPLICATION

LREP DAVIDSON, DAVIDSON & KAPPEL, LLC, 485 SEVENTH AVENUE, 14TH FLOOR, NEW YORK, NY, 10018

CLMN Number of Claims: 34

ECL Exemplary Claim: 1

DRWN 2 Drawing Page(s)

LN.CNT 807

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention relates to compounds, which are phospholipid derivatives of valproic acid, to compositions comprising said compounds and their use for treating epilepsy, migraine, **bipolar** disorders and pain.

L23 ANSWER 3 OF 7 USPATFULL on STN

AN 2003:258300 USPATFULL

TI Composition & use as analgesic, anti-inflammatory, wound healing agent, for treatment of heart conditions, assessment of heart function & tissue & cell protection & healing & reperfusion, mood disorders & symptoms & sequelae of menopause & for inducing unconsciousness, sleep & anesthesia

IN Nyce, Jonathan W., Titusville, NJ, UNITED STATES

PI US 2003181353 A1 20030925

AI US 2003-349219 A1 20030121 (10)

RLI Division of Ser. No. US 2001-762090, filed on 1 Feb 2001, ABANDONED A 371 of International Ser. No. WO 1999-US17642, filed on 3 Aug 1999, PENDING

PRAI US 1998-95090P 19980803 (60)

DT Utility

FS APPLICATION

LREP HOWREY SIMON ARNOLD & WHITE, LLP, BOX 34, 301 RAVENSWOOD AVE., MENLO PARK, CA, 94025

CLMN Number of Claims: 108

ECL Exemplary Claim: 95

DRWN No Drawings

LN.CNT 1818

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Composition and formulations comprise a brain, heart, lung and/or vascular system protecting amount of a first agent such as folinic acid, pharmaceutically acceptable salts thereof or mixtures thereof and a carrier, and optionally a second agent such as analgesics, heart medicines, anti-inflammatory agents, soporifics, muscle relaxants, anti-pyretic agents, anti-fibrillation agents, heart, brain, lung and vascular drugs, anxiolytic agents, mood controlling agents, and many others. The products are suitable for the treatment of previous mood disorders, symptoms and sequelae of menopause, pain, inflammation, insomnia, restless sleep, trauma, surgery, burns, conditions and diseases which bring these symptoms, ischemia, Supra Ventricular Tachycardia (SVT), heart conditions and heart failure, Acute Respiratory Distress Syndrome (ARDS), COPD, allergic rhinitis, and other conditions, and for reducing the number and severity of heart attacks, as well as for alleviating other diseases associated with the heart, and more generally, for the assessment of heart function. An edible product is prepared with the agent of the invention.

L23 ANSWER 4 OF 7 USPATFULL on STN

AN 2003:17078 USPATFULL

TI Omega-3 fatty acids in the treatment of depression

IN Stoll, Andrew, Lincoln, MA, UNITED STATES

PI US 2003012827 A1 20030116

AI US 2002-83913 A1 20020227 (10)

RLI Continuation-in-part of Ser. No. US 1999-269361, filed on 22 Mar 1999, GRANTED, Pat. No. US 6344482 A 371 of International Ser. No. WO 1997-US6712, filed on 23 Apr 1997, PENDING

DT Utility

FS APPLICATION

LREP Choate, Hall & Stewart, Exchange Place, 53 State Street, Boston, MA, 02109

CLMN Number of Claims: 27

ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 617

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention is directed to a method of treating patients with major depression by administering omega-3 fatty acids. These may be administered in a substantially purified form, as part of a pharmaceutical composition, or as part of a larger molecule, e.g., a triacylglycerol, which releases free fatty acid after ingestion by a patient.

The present invention is also directed to triacylglycerols which are esterified at the gamma carbon of glycerol to phosphocholine and at either the alpha or beta carbon of glycerol to an omega-3 fatty acid. These "omega-3 phosphatidylcholines" are also used in the treatment of patients with major depression.

L23 ANSWER 5 OF 7 USPATFULL on STN

AN 2002:172346 USPATFULL

TI Omega-3 fatty acids and omega-3 phosphatidylcholine in the treatment of **bipolar** disorder

IN Stoll, Andrew L., Lincoln, MA, UNITED STATES

Severus, Wolfram E., Berlin, GERMANY, FEDERAL REPUBLIC OF

PI US 2002091103 A1 20020711

AI US 2002-68035 A1 20020205 (10)
RLI Continuation of Ser. No. US 1999-269361, filed on 22 Mar 1999, PATENTED
PRAI WO 1997-US6712 19970423
DT Utility
FS APPLICATION
LREP Choate, Hall & Stewart, Exchange Place, 53 State Street, Boston, MA,
02109
CLMN Number of Claims: 25
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 439

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention is directed to a method of treating patients with **bipolar** disorder by administering omega-3 fatty acids. These may be administered in a substantially purified form, as part of a pharmaceutical composition, or as part of a larger molecule, e.g. a triacylglycerol, which releases free fatty acid after ingestion by a patient.

The present invention is also directed to triacylglycerols which are esterified at the gamma carbon of glycerol to phosphocholine and at either the alpha or beta carbon of glycerol to an omega-3 fatty acid. These "omega-3 phosphatidylcholines" are also used in the treatment of patients with **bipolar** disorder.

L23 ANSWER 6 OF 7 USPATFULL on STN

AN 2002:48595 USPATFULL

TI METHODS FOR INCREASING CYTIDINE LEVELS IN VIVO AND TREATING
CYTIDINE-DEPENDENT HUMAN DISEASES

IN WATKINS, CAROL, CAMBRIDGE, MA, UNITED STATES
WURTMAN, RICHARD J., BOSTON, MA, UNITED STATES

PI US 2002028787 A1 20020307

AI US 1999-363748 A1 19990730 (9)

PRAI US 1998-95002P 19980731 (60)

DT Utility

FS APPLICATION

LREP PATENT ADMINISTRATOR, KATTEN MUCHIN ZAVIS, SUITE 1600, 525 WEST MONROE
STREET, CHICAGO, IL, 60661

CLMN Number of Claims: 38

ECL Exemplary Claim: 1

DRWN 3 Drawing Page(s)

LN.CNT 612

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Methods of treating certain neurological diseases using exogenous uridine or a uridine source alone as a precursor of endogenous cytidine, particularly in the human brain, are disclosed. Methods are also disclosed wherein exogenous uridine or a uridine source is combined either with drugs increasing uridine availability or with compounds that serve as a source of choline in phospholipid synthesis.

L23 ANSWER 7 OF 7 USPATFULL on STN

AN 2002:24309 USPATFULL

TI Omega-3 fatty acids in the treatment of **bipolar** disorder

IN Stoll, Andrew L., 35 Old Winter St., Lincoln, MA, United States 01773
Severus, Wolfram E., Badensche Strasse 7, D-10825 Berlin, GERMANY,
FEDERAL REPUBLIC OF

PI US 6344482 B1 20020205

AI WO 9739759 19971030
US 1999-269361 19990322 (9)
WO 1997-US6712 19970423
19990322 PCT 371 date

DT Utility
FS GRANTED

EXNAM Primary Examiner: Jarvis, William R. A.
LREP Choate, Hall & Stewart
CLMN Number of Claims: 9
ECL Exemplary Claim: 1
DRWN 0 Drawing Figure(s); 0 Drawing Page(s)
LN.CNT 387

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention is directed to a method of treating patients with
bipolar disorder by administering omega-3 fatty acids.

Lithium to treat Bipolar disorder

Cook 10/068,035

June 25, 2004

=> d que

L15 2068 SEA FILE=HCAPLUS ABB=ON PLU=ON "MENTAL DISORDER (L) BIPOLAR
DISORDER"+OLD/CT
L24 1 SEA FILE=REGISTRY ABB=ON PLU=ON LITHIUM/CN
L25 74563 SEA FILE=HCAPLUS ABB=ON PLU=ON LITHIUM/CT
L26 74563 SEA FILE=HCAPLUS ABB=ON PLU=ON L24 OR L25
L27 1863 SEA FILE=HCAPLUS ABB=ON PLU=ON L26(L) (BAC OR DMA OR PAC OR
PKT OR THU)/RL
L28 297 SEA FILE=HCAPLUS ABB=ON PLU=ON L27 AND L15
L29 21 SEA FILE=HCAPLUS ABB=ON PLU=ON L28 AND P/DT
L30 276 SEA FILE=HCAPLUS ABB=ON PLU=ON L28 NOT L29
L31 77 SEA FILE=HCAPLUS ABB=ON PLU=ON L30 AND PY<1999
L32 20 SEA FILE=HCAPLUS ABB=ON PLU=ON L31 AND REVIEW/DT
L33 7 SEA FILE=HCAPLUS ABB=ON PLU=ON L32 AND (LI OR LITHIUM)/TI
AND BIPOL?/TI

=> d l33 ibib abs hitind hitstr 1-7

L33 ANSWER 1 OF 7 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1998:740935 HCAPLUS

DOCUMENT NUMBER: 130:148033

TITLE: Glycogen synthase kinase-3 - a new target for
lithium's effects in bipolar
patients?

AUTHOR(S): Agam, Galila; Levine, Joseph

CORPORATE SOURCE: Faculty of Health Science, Ben-Gurion University,
Beersheva, Israel

SOURCE: Human Psychopharmacology (1998), 13(7),
463-465

CODEN: HUPSEC; ISSN: 0885-6222

PUBLISHER: John Wiley & Sons Ltd.

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review with 15 refs. on the possibility that lithium's therapeutic
effect is mediated via inhibition of glycogen synthase kinase-3 in
treatment of bipolar disorders.

CC 1-0 (Pharmacology)

IT Mental disorder

(manic bipolar disorder; glycogen
synthase kinase-3 as new target for lithium's effects in bipolar human
patients)

IT 7439-93-2, Lithium, biological studies

RL: BAC (Biological activity or effector, except adverse); BSU
(Biological study, unclassified); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)

(glycogen synthase kinase-3 as new target for lithium's effects in
bipolar human patients)

IT 7439-93-2, Lithium, biological studies

RL: BAC (Biological activity or effector, except adverse); BSU
(Biological study, unclassified); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)

(glycogen synthase kinase-3 as new target for lithium's effects in
bipolar human patients)

RN 7439-93-2 HCAPLUS

CN Lithium (7CI, 8CI, 9CI) (CA INDEX NAME)

Li

REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L33 ANSWER 2 OF 7 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1998:454808 HCAPLUS

DOCUMENT NUMBER: 129:197460

TITLE: Behavioral reversal of **lithium** effects by
four inositol isomers correlates perfectly with
biochemical effects on the PI cycle: depletion by
chronic **lithium** of brain inositol is
specific to hypothalamus, and inositol levels may be
abnormal in postmortem brain from **bipolar**
patients

AUTHOR(S): Belmaker, Robert H.; Agam, Galila; Van Calker,
Dietrich; Richards, Mary H.; Kofman, Ora

CORPORATE SOURCE: Ministry of Health Mental Health Center, Faculty of
Health Sciences Ben Gurion University of the Negev,
Beersheva, Israel

SOURCE: Neuropsychopharmacology (1998), 19(3),
220-232

CODEN: NEROEW; ISSN: 0893-133X

PUBLISHER: Elsevier Science Inc.

DOCUMENT TYPE: Journal; **General Review**

LANGUAGE: English

AB A review with 62 refs. The inositol depletion hypothesis of lithium (Li) action has been criticized, because depletion of inositol after chronic Li treatment has not been reproducible, effects of inositol to reverse Li-induced behaviors occurred also with epi-inositol, a unnatural isomer, and because inositol is ubiquitous in brain and hard to relate to the pathogenesis of affective disorder. Therefore, we review our studies showing that lithium depletion of brain inositol occurs chronically in the hypothalamus, a region not previously examined; that behavioral effects of four different inositol isomers including epi-inositol correlate perfectly with their biochem. effects; and that inositol in postmortem human brain is reduced by 25% in frontal cortex of bipolars and suicides as compared with controls. Because inositol in postmortem brain is reduced and not increased in bipolar patients, the relationship between inositol, lithium, and affective disorder is complex.

CC 1-0 (Pharmacology)

Section cross-reference(s): 14

IT **Mental disorder**

(**manic bipolar disorder**; lithium
behavioral effects reversed by four inositol isomers in relation to
biochem. effects on PI cycle in rat brain and inositol levels in
postmortem bipolar humans)

IT 7439-93-2, Lithium, biological studies

RL: BAC (**Biological activity or effector, except adverse**); BSU(Biological study, unclassified); THU (**Therapeutic use**); BIOL

(Biological study); USES (Uses)

(lithium behavioral effects reversed by four inositol isomers in
relation to biochem. effects on PI cycle in rat brain and inositol
levels in postmortem bipolar humans)

IT 7439-93-2, Lithium, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU
(Biological study, unclassified); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)
(lithium behavioral effects reversed by four inositol isomers in
relation to biochem. effects on PI cycle in rat brain and inositol
levels in postmortem bipolar humans)
RN 7439-93-2 HCAPLUS
CN Lithium (7CI, 8CI, 9CI) (CA INDEX NAME)

Li

REFERENCE COUNT: 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L33 ANSWER 3 OF 7 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1998:454802 HCAPLUS

DOCUMENT NUMBER: 129:211123

TITLE: **Lithium: a molecular transducer of
mood-stabilization in the treatment of bipolar
disorder**

AUTHOR(S): Manji, Hussein K.; Lenox, Robert H.

CORPORATE SOURCE: Departments of Psychiatry and Behavioral
Neurosciences, and Pharmacology, Molecular
Pathophysiology Program, Wayne State University School
of Medicine, Detroit, MI, USA

SOURCE: Neuropsychopharmacology (1998), 19(3),
161-166

CODEN: NEROEW; ISSN: 0893-133X

PUBLISHER: Elsevier Science Inc.

DOCUMENT TYPE: Journal; **General Review**

LANGUAGE: English

AB A review with 42 refs. This article reviews data regarding the mechanism
of action of lithium in bipolar disorder.

CC 1-0 (Pharmacology)

IT **Mental disorder**
(**manic bipolar disorder**; lithium mol.
mechanisms in mood-stabilization in treatment of humans with
bipolar disorder)

IT 7439-93-2, Lithium, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU
(Biological study, unclassified); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)
(lithium mol. mechanisms in mood-stabilization in treatment of humans
with bipolar disorder)

IT 7439-93-2, Lithium, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU
(Biological study, unclassified); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)
(lithium mol. mechanisms in mood-stabilization in treatment of humans
with bipolar disorder)

RN 7439-93-2 HCAPLUS

CN Lithium (7CI, 8CI, 9CI) (CA INDEX NAME)

Li

REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L33 ANSWER 4 OF 7 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1998:305315 HCAPLUS

DOCUMENT NUMBER: 129:49066

TITLE: Recurrence risk in **bipolar** manic-depressive
disorders after discontinuing **lithium**
maintenance treatment: an overview

AUTHOR(S): Baldessarini, Ross J.; Tondo, Leonardo

CORPORATE SOURCE: Laboratories for Psychiatric Research, McLean Division
of Massachusetts General Hospital, Harvard Medical
School, Belmont, MA, USASOURCE: Clinical Drug Investigation (1998), 15(4),
337-351

CODEN: CDINFR; ISSN: 1173-2563

PUBLISHER: Adis International Ltd.

DOCUMENT TYPE: Journal; **General Review**

LANGUAGE: English

AB A review with 80 refs. Lithium remains unequalled in its research support as a standard maintenance treatment for bipolar manic-depressive disorders. It has important beneficial effects on recurring bipolar depression as well as mania, and in both types I and II bipolar syndromes, with powerful antisuicide effects not demonstrated with alternative mood-stabilizers. Numerous studies indicate that discontinuing lithium maintenance treatment is followed by sharply increased morbidity and possibly mortality, particularly in the 1st 6-12 mo. However, gradual discontinuation markedly reduces, and not merely delays, recurrences of mania or depression after discontinuing lithium, with an even stronger effect in bipolar type II than type I patients. Secondary long-term retreatment with lithium following discontinuation yields only minor average losses of benefits. Increased early recurrence risk may also arise after stopping long-term treatment with other neuropsychotropic drugs. Such reactions probably reflect physiol. adaptations of the brain to pharmacodynamic effects, and their impact may be limited by slow drug discontinuation. The phenomenon of high early post-treatment discontinuation recurrence risk has clin. and scientific implications for the design, management and interpretation of treatment protocols that involve discontinuing long-term treatments in disorders requiring maintenance pharmacotherapy with centrally neuropharmacol. active drugs.

CC 1-0. (Pharmacology)

IT **Mental disorder**

(**manic bipolar disorder**; recurrence risk
in bipolar manic-depressive disorders of humans after discontinuing
lithium maintenance treatment)

IT 7439-93-2, Lithium, biological studies

RL: ADV (Adverse effect, including toxicity); **BAC (Biological
activity or effector, except adverse)**; BSU (Biological study,
unclassified); **THU (Therapeutic use)**; BIOL (Biological study);
USES (Uses)

(recurrence risk in bipolar manic-depressive disorders of humans after
discontinuing maintenance treatment with)

IT 7439-93-2, Lithium, biological studies

RL: ADV (Adverse effect, including toxicity); **BAC (Biological**

activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use);** BIOL (Biological study); USES (Uses)

(recurrence risk in bipolar manic-depressive disorders of humans after discontinuing maintenance treatment with)

RN 7439-93-2 HCAPLUS

CN Lithium (7CI, 8CI, 9CI) (CA INDEX NAME)

Li

REFERENCE COUNT: 80 THERE ARE 80 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L33 ANSWER 5 OF 7 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1998:105090 HCAPLUS

DOCUMENT NUMBER: 128:212508

TITLE: Use of **lithium** in **bipolar** disorder

AUTHOR(S): Young, Robert C.

CORPORATE SOURCE: Department of Psychiatry, Westchester Division, The New York Hospital-Cornell Medical Center, White Plains, NY, USA

SOURCE: Medical Psychiatry (1998), 9(Geriatric Psychopharmacology), 259-272

CODEN: MEPSEN

PUBLISHER: Marcel Dekker, Inc.

DOCUMENT TYPE: Journal; **General Review**

LANGUAGE: English

AB A review with 52 refs. Somatic treatments that are effective for bipolar depression in younger patients can also be effective in the elderly. This chapter focuses on treatment of geriatric manic and depressed bipolar patients with lithium salts directed at acute suppression of symptoms, continuation treatment to prevent immediate relapse, and long term maintenance.

CC 1-0 (Pharmacology)

IT **Mental disorder**
(depression; lithium treatment of **bipolar disorder** in geriatric humans)

IT **Mental disorder**
(mania; lithium treatment of **bipolar disorder** in geriatric humans)

IT **Mental disorder**
(**manic bipolar disorder**; lithium treatment of **bipolar disorder** in geriatric humans)

IT 7439-93-2, Lithium, biological studies

RL: ADV (Adverse effect, including toxicity); **BAC (Biological activity or effector, except adverse);** BSU (Biological study, unclassified); **THU (Therapeutic use);** BIOL (Biological study); USES (Uses)

(lithium treatment of bipolar disorder in geriatric humans)

IT 7439-93-2, Lithium, biological studies

RL: ADV (Adverse effect, including toxicity); **BAC (Biological activity or effector, except adverse);** BSU (Biological study, unclassified); **THU (Therapeutic use);** BIOL (Biological study); USES (Uses)

(lithium treatment of bipolar disorder in geriatric humans)

RN 7439-93-2 HCAPLUS
CN Lithium (7CI, 8CI, 9CI) (CA INDEX NAME)

Li

REFERENCE COUNT: 75 THERE ARE 75 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L33 ANSWER 6 OF 7 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1998:88534 HCAPLUS

DOCUMENT NUMBER: 128:212458

TITLE: Lithium plus valproate as maintenance
polypharmacy for patients with bipolar I
disorder: a review

AUTHOR(S): Solomon, David A.; Keitner, Gabor I.; Ryan, Christine
E.; Miller, Ivan W.

CORPORATE SOURCE: Department of Psychiatry and Human Behavior, Rhode
Island Hospital, Providence, RI, 02903, USA

SOURCE: Journal of Clinical Psychopharmacology (1998
) , 18(1), 38-49

CODEN: JCPYDR; ISSN: 0271-0749

PUBLISHER: Williams & Wilkins

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review with 99 refs. Standard pharmacotherapy for the maintenance treatment of patients with bipolar I disorder consists of lithium, valproate, or carbamazepine. However, many patients fail to respond to monotherapy with any of these agents, and as a result, psychiatrists often resort to polypharmacy. Findings from some open-label trials and retrospective chart reviews suggest this approach may be useful, but in the few controlled trials that have been conducted, the results have been neg. One drug combination that warrants further study as maintenance therapy is lithium plus valproate. Each is approved by the U.S. Food and Drug Administration for treatment of acute mania, and lithium has demonstrated efficacy for maintenance treatment as well. Some preliminary evidence suggests that the combination can be effective for patients who do not respond to monotherapy, and it seems to be no more dangerous than monotherapy. Concomitant administration of lithium plus valproate does not significantly alter lithium pharmacokinetics, and statistically significant changes that arise in valproate pharmacokinetics are not clin. significant. Although it is not known whether the drugs interact to augment response, many of their effects in the central nervous system do differ, and there is no indication of pharmacodynamic interactions that oppose each other. Finally, some evidence suggests that lithium and valproate may differ with regard to clin. variables that predict response to treatment.

CC 1-0 (Pharmacology)

IT Mental disorder

(manic bipolar disorder;

Lithium/valproate maintenance polypharmacy for humans with bipolar I disorder)

IT 99-66-1 7439-93-2, Lithium, biological studies

RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study);

USES (Uses)
(Lithium/valproate maintenance polypharmacy for humans with bipolar I disorder)

IT 7439-93-2, Lithium, biological studies
RL: ADV (Adverse effect, including toxicity); **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study);
USES (Uses)
(Lithium/valproate maintenance polypharmacy for humans with bipolar I disorder)

RN 7439-93-2 HCAPLUS
CN Lithium (7CI, 8CI, 9CI) (CA INDEX NAME)

Li

REFERENCE COUNT: 99 THERE ARE 99 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L33 ANSWER 7 OF 7 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1995:713254 HCAPLUS
DOCUMENT NUMBER: 123:131800
TITLE: Inositol monophosphatase -- a putative target for **Li+** in the treatment of **bipolar** disorder
AUTHOR(S): Atack, John R.; Broughton, Howard B.; Pollack, Scott J.
CORPORATE SOURCE: Merck Sharp Dohme Res. Lab., Neurosci. Res. Cent., Harlow, Essex, CM20 2QR, UK
SOURCE: Trends in Neurosciences (1995), 18(8), 343-9
CODEN: TNSCDR; ISSN: 0166-2236
PUBLISHER: Elsevier Trends Journals
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English

AB A review, with 97 refs., discussing the hypothesis that attenuation of the phosphatidylinositol signal transduction pathway as a consequence of inhibition of inositol monophosphatase is the mechanism for the efficacy of **Li+** in the treatment of bipolar disorder.

CC 1-0 (Pharmacology)

IT **Mental disorder**
(**manic bipolar disorder**, inositol monophosphatase as target for lithium in treatment of bipolar disease)

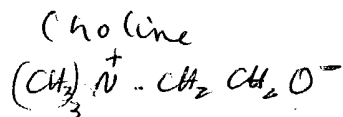
IT 7439-93-2, Lithium, biological studies
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(inositol monophosphatase as target for lithium in treatment of bipolar disease)

IT 7439-93-2, Lithium, biological studies
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(inositol monophosphatase as target for lithium in treatment of bipolar disease)

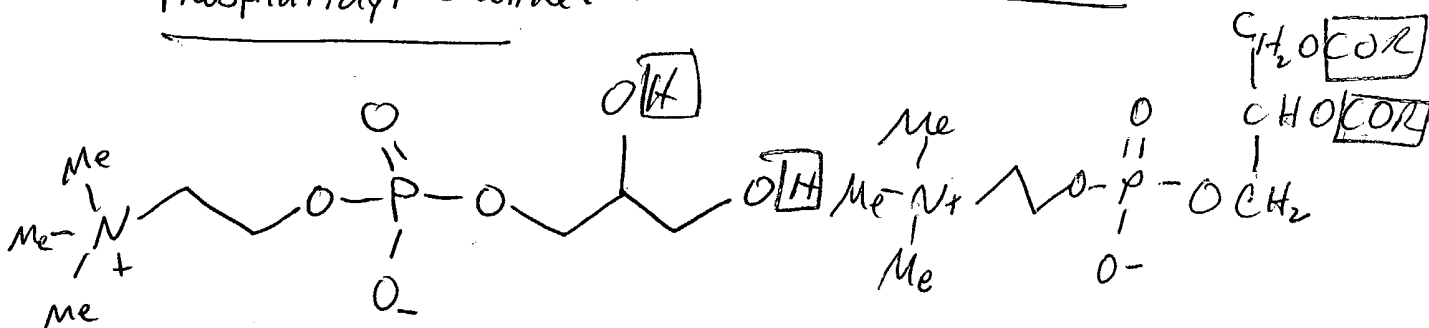
RN 7439-93-2 HCAPLUS
CN Lithium (7CI, 8CI, 9CI) (CA INDEX NAME)

Li

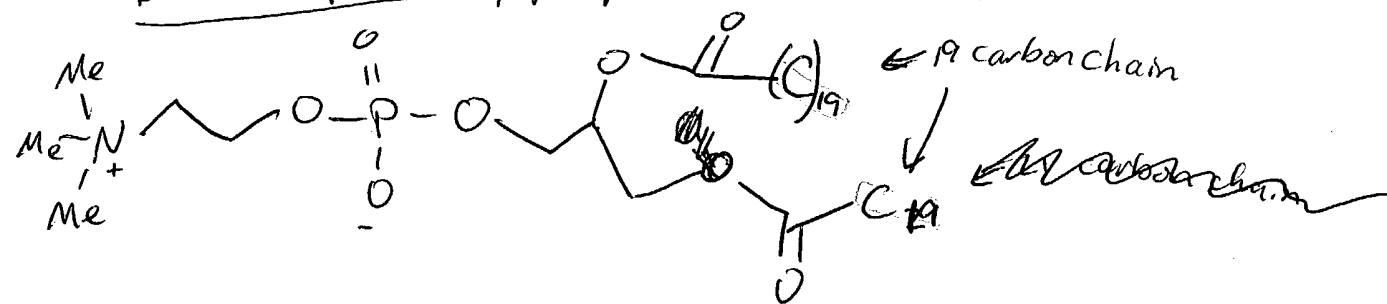
Basic Structure of Phosphatidyl Choline:



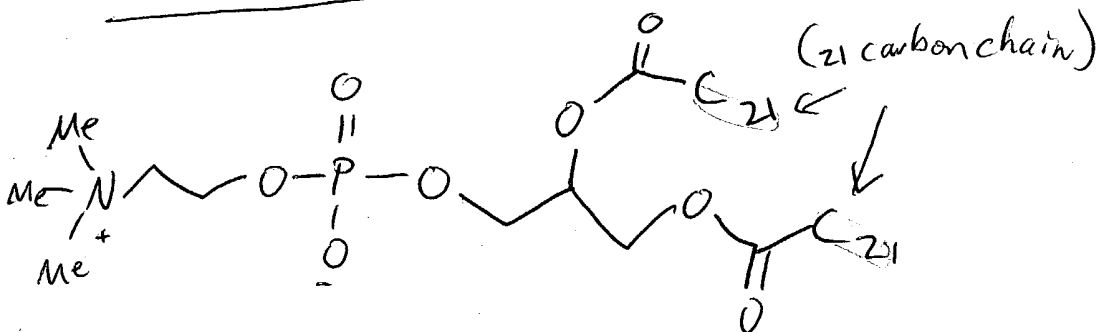
Lecithin



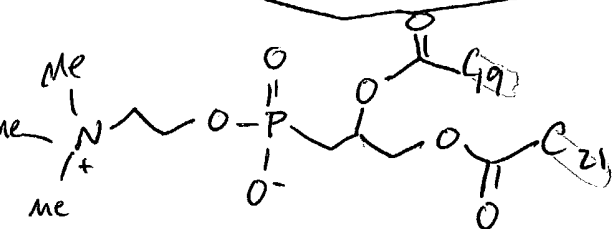
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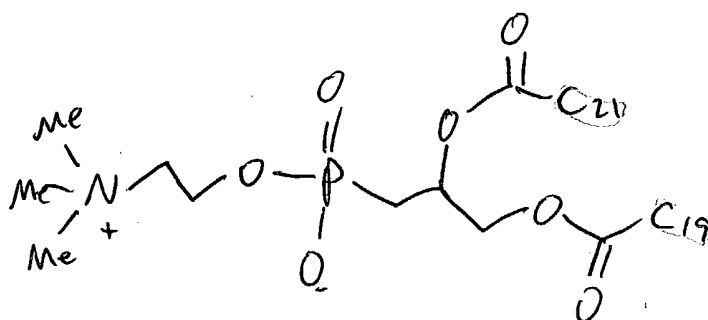
Didocosahexanoyl "



1-eicosapent..., 2-docosahex....



1-docosahex..., 2-eicosapent....



L6 ANSWER 1 OF 2 REGISTRY COPYRIGHT 2004 ACS on STN
RN 28319-77-9 REGISTRY
CN Ethanaminium, 2-[[[(2R)-2,3-dihydroxypropoxy]hydroxyphosphinyl]oxy]-N,N,N-trimethyl-, inner salt (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN Choline, hydroxide, 2,3-dihydroxypropyl hydrogen phosphate, inner salt, D-(8CI)
CN Ethanaminium, 2-[[[(2,3-dihydroxypropoxy)hydroxyphosphinyl]oxy]-N,N,N-trimethyl-, hydroxide, inner salt, (R)-

OTHER NAMES:

CN Brezal
CN Choline alfoscerate
CN Delecit
CN Ethanaminium, 2-[[[(2,3-dihydroxypropoxy)hydroxyphosphinyl]oxy]-N,N,N-trimethyl-, inner salt, (R)-
CN Gliatilin
CN Glycerophosphocholine
CN Glycerophosphorylcholine
CN L- α -Glycerophosphocholine
CN L- α -Glycerophosphorylcholine
CN L- α -Glycerylphosphorylcholine
CN L- α -GPC
CN L- α -Lecithin
CN ~~L- α -Phosphatidylcholine~~
CN O-(sn-glycero-3-Phosphoryl)-choline
CN sn-Glycero-3-phosphocholine
CN sn-Glycero-3-phosphorylcholine
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DR 103709-68-8, 117829-79-5
MF C8 H20 N O6 P
CI COM

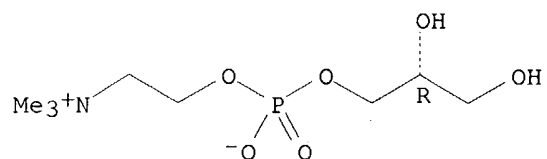
LC STN Files: ADISINSIGHT, AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CAPLUS, CASREACT, CEN, CHEMCATS, CHEMLIST, CSChem, DDFU, DRUGU, EMBASE, IMSRESEARCH, IPA, MRCK*, PHAR, PROMT, PROUSDDR, RTECS*, TOXCENTER, USAN, USPAT2, USPATFULL
(*File contains numerically searchable property data)

Other Sources: EINECS**, WHO

(**Enter CHEMLIST File for up-to-date regulatory information)

DT.CA Caplus document type: Conference; Journal; Patent
RL.P Roles from patents: ANST (Analytical study); BIOL (Biological study); PREP (Preparation); PROC (Process); RACT (Reactant or reagent); USES (Uses)
RLD.P Roles for non-specific derivatives from patents: BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
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Absolute stereochemistry.



376 REFERENCES IN FILE CA (1907 TO DATE)

42 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

378 REFERENCES IN FILE CAPLUS (1907 TO DATE)

Inventors

Cook 10/068,035

June 25, 2004

L13 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1997:717821 HCAPLUS

DOCUMENT NUMBER: 128:7311

ENTRY DATE: Entered STN: 13 Nov 1997

TITLE: Fatty acids and **phosphatidylcholines** in the treatment of bipolar disorder

INVENTOR(S): **Stoll, Andrew L.; Severus, Wolfram E.**

PATENT ASSIGNEE(S): Brigham and Women's Hospital, USA; Stoll, Andrew L.; Severus, Wolfram E.

SOURCE: PCT Int. Appl., 13 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

INT. PATENT CLASSIF.:

MAIN: A61K033-14

SECONDARY: A61K031-66; A61K031-20

CLASSIFICATION: 63-6 (Pharmaceuticals)

Section cross-reference(s): 1

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9739759	A2	19971030	WO 1997-US6712	19970423
WO 9739759	A3	19980115		
W: AU, CA, JP, US				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9727384	A1	19971112	AU 1997-27384	19970423
US 6344482	B1	20020205	US 1999-269361	19990322
US 2002091103	A1	20020711	US 2002-68035	20020205
US 2003012827	A1	20030116	US 2002-83913	20020227
PRIORITY APPLN. INFO.:		US 1996-16140P	P	19960424
		WO 1997-US6712	W	19970423
		US 1999-269361	A1	19990322

ABSTRACT:

The present invention is directed to a method of treating patients with bipolar disorder by administering ω -3 fatty acids. These may be administered in a substantially purified form, as part of a pharmaceutical composition, or as part of a larger mol., e.g. a triacylglycerol, which releases free fatty acid after ingestion by a patient. The present invention is also directed to triacylglycerols which are esterified at the γ -carbon of glycerol with phosphocholine and at either the α - or β -carbon of glycerol with an ω -3 fatty acid. These ω -3 **phosphatidylcholines** are also used in the treatment of patients with bipolar disorder.

SUPPL. TERM: polyunsatd fatty acid **phosphatidylcholine** bipolar disorder

INDEX TERM: Mental disorder
(manic bipolar disorder; ω -3 fatty acids and **phosphatidylcholines** for treatment of bipolar disorder)

INDEX TERM: Drug delivery systems
(oral; ω -3 fatty acids and **phosphatidylcholines** for treatment of bipolar disorder)

INDEX TERM: Fatty acids, biological studies
ROLE: BAC (Biological activity or effector, except adverse);
BSU (Biological study, unclassified); THU (Therapeutic use);
BIOL (Biological study); USES (Uses)
(polyunsatd., n-3; ω -3 fatty acids and
phosphatidylcholines for treatment of bipolar
disorder)

INDEX TERM: **Phosphatidylcholines**, biological studies
ROLE: BAC (Biological activity or effector, except adverse);
BSU (Biological study, unclassified); THU (Therapeutic use);
BIOL (Biological study); USES (Uses)
(ω -3 fatty acids and **phosphatidylcholines**
for treatment of bipolar disorder)

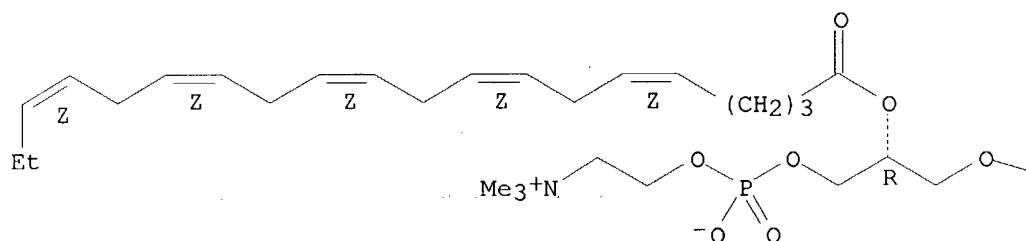
INDEX TERM: 7439-93-2D, Lithium, compds., biological studies
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BSU (Biological study, unclassified); THU (Therapeutic use);
BIOL (Biological study); USES (Uses)
(as addnl. agent; ω -3 fatty acids and
phosphatidylcholines for treatment of bipolar
disorder)

INDEX TERM: 6217-54-5, Docosahexaenoic acid 10417-94-4,
Eicosapentaenoic acid 87879-23-0 87879-27-4 98819-78-4
198779-10-1
ROLE: BAC (Biological activity or effector, except adverse);
BSU (Biological study, unclassified); THU (Therapeutic use);
BIOL (Biological study); USES (Uses)
(ω -3 fatty acids and **phosphatidylcholines**
for treatment of bipolar disorder)

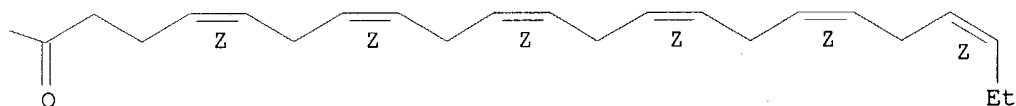
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 RN 198779-10-1 REGISTRY
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 4-hydroxy-N,N,N-trimethyl-10-oxo-7-[(1-oxo-5,8,11,14,17-
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 NAME)
 FS STEREOSEARCH
 MF C50 H78 N O8 P
 SR CA
 LC STN Files: CA, CAPLUS, USPATFULL
 DT.CA Caplus document type: Patent
 RL.P Roles from patents: BIOL (Biological study); USES (Uses)

Absolute stereochemistry.
 Double bond geometry as shown.

PAGE 1-A



PAGE 1-B



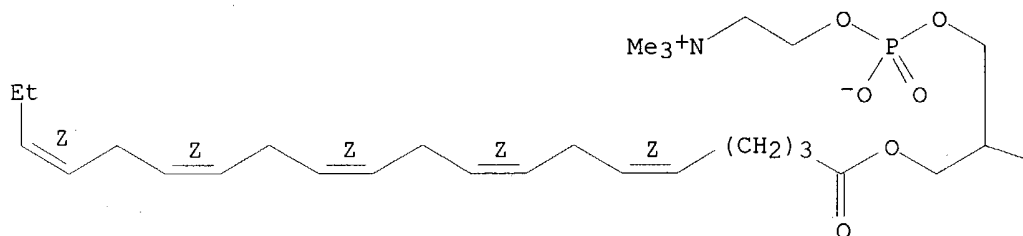
1 REFERENCES IN FILE CA (1907 TO DATE)
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L14 ANSWER 2 OF 7 REGISTRY COPYRIGHT 2004 ACS on STN
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 (14Z,17Z,20Z,23Z,26Z)- (9CI) (CA INDEX NAME)
 OTHER CA INDEX NAMES:
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 FS STEREOSEARCH
 MF C48 H76 N O8 P

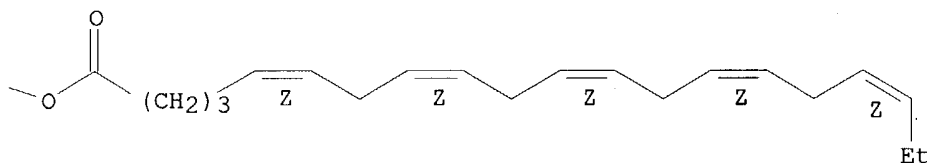
SR CA
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 DT.CA CAplus document type: Journal; Patent
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Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

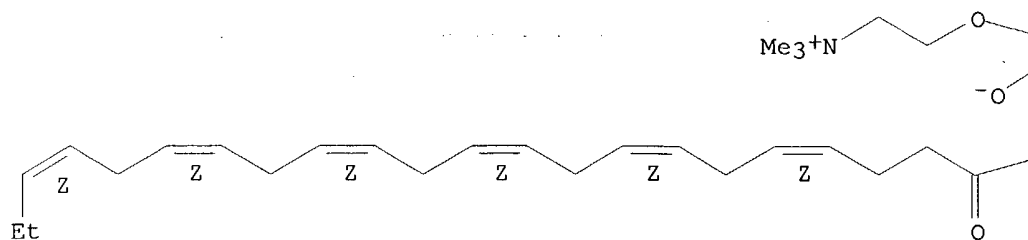


5 REFERENCES IN FILE CA (1907 TO DATE)
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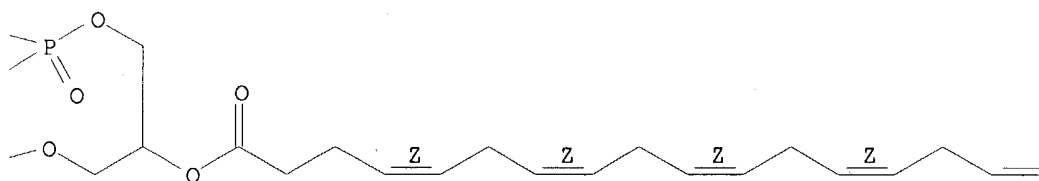
L14 ANSWER 3 OF 7 REGISTRY COPYRIGHT 2004 ACS on STN
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 OTHER CA INDEX NAMES:
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 FS STEREOSEARCH
 MF C52 H80 N O8 P
 LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL
 DT.CA CAplus document type: Journal; Patent
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Double bond geometry as shown.

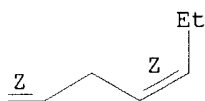
PAGE 1-A



PAGE 1-B



PAGE 1-C



12 REFERENCES IN FILE CA (1907 TO DATE)
 12 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L14 ANSWER 4 OF 7 REGISTRY COPYRIGHT 2004 ACS on STN

RN 87879-23-0 REGISTRY

CN 3,5,8-Trioxa-4-phosphatriaconta-12,15,18,21,24,27-hexaen-1-aminium,
 4-hydroxy-N,N,N-trimethyl-9-oxo-7-[[[(5Z,8Z,11Z,14Z,17Z)-1-oxo-
 5,8,11,14,17-eicosapentaenyl]oxy]methyl]-, inner salt, 4-oxide,
 (12Z,15Z,18Z,21Z,24Z,27Z)- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN 3,5,8-Trioxa-4-phosphatriaconta-12,15,18,21,24,27-hexaen-1-aminium,
 4-hydroxy-N,N,N-trimethyl-9-oxo-7-[[[(1-oxo-5,8,11,14,17-
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FS STEREOSEARCH

MF C50 H78 N O8 P

LC STN Files: CA, CAPLUS, USPATFULL

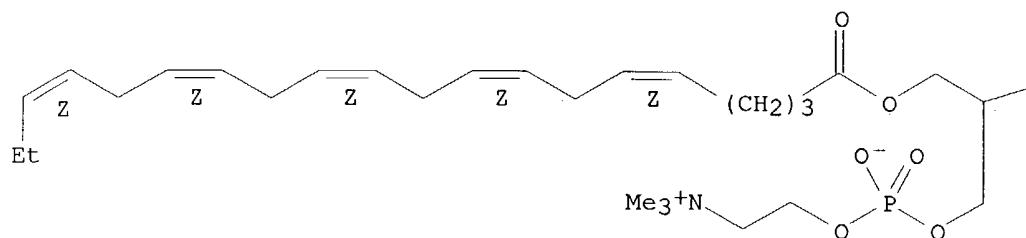
DT.CA Caplus document type: Journal; Patent

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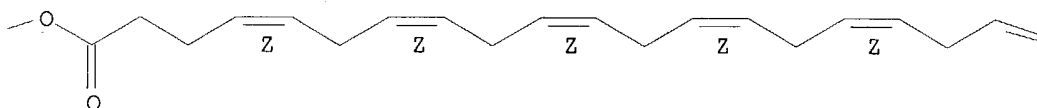
RL.NP Roles from non-patents: BIOL (Biological study); OCCU (Occurrence)

Double bond geometry as shown.

PAGE 1-A



PAGE 1-B



PAGE 1-C



4 REFERENCES IN FILE CA (1907 TO DATE)
4 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L14 ANSWER 5 OF 7 REGISTRY COPYRIGHT 2004 ACS on STN

RN 10417-94-4 REGISTRY

CN 5,8,11,14,17-Eicosapentaenoic acid, (5Z,8Z,11Z,14Z,17Z)- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN 5,8,11,14,17-Eicosapentaenoic acid (6CI)

CN 5,8,11,14,17-Eicosapentaenoic acid, (all-Z)- (8CI)

OTHER NAMES:

CN (5Z,8Z,11Z,14Z,17Z)-Eicosapentaenoic acid

CN (all-cis)-5,8,11,14,17-Eicosapentaenoic acid

CN (all-Z)-Δ5,8,11,14,17-Eicosapentaenoic acid

CN (all-Z)-5,8,11,14,17-Eicosapentaenoic acid

CN Eicosapentaenoic acid

CN EPA

CN Icosapent

CN Icosapentaenoic acid

CN Timnodonic acid

FS STEREOSEARCH

DR 25377-48-4
MF C20 H30 O2
CI COM

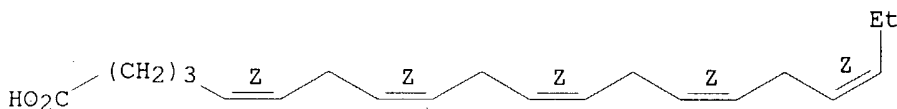
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(*File contains numerically searchable property data)

Other Sources: WHO

DT.CA Caplus document type: Conference; Dissertation; Journal; Patent; Report
RL.P Roles from patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); OCCU (Occurrence); PREP (Preparation); PROC (Process); RACT (Reactant or reagent); USES (Uses)
RLD.P Roles for non-specific derivatives from patents: BIOL (Biological study); OCCU (Occurrence); PREP (Preparation); PROC (Process); RACT (Reactant or reagent); USES (Uses)
RL.NP Roles from non-patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); MSC (Miscellaneous); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses); NORL (No role in record)
RLD.NP Roles for non-specific derivatives from non-patents: ANST (Analytical study); BIOL (Biological study); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)

Double bond geometry as shown.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

7667 REFERENCES IN FILE CA (1907 TO DATE)
176 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
7679 REFERENCES IN FILE CAPLUS (1907 TO DATE)
6 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

L14 ANSWER 6 OF 7 REGISTRY COPYRIGHT 2004 ACS on STN

RN 7439-93-2 REGISTRY

CN Lithium (7CI, 8CI, 9CI) (CA INDEX NAME)

OTHER NAMES:

CN Lithium atom

CN Lithium element

MF Li

CI COM

LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, AQUIRE, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMINFORMRX, CHEMLIST, CIN, CSCHM, CSNB, DDFU, DETHERM*, DIPPR*, DRUGU, EMBASE, ENCOMPLIT, ENCOMPLIT2, ENCOMPPAT, ENCOMPPAT2, HSDB*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, MSDS-OHS, NIOSHTIC, PIRA, PROMT, RTECS*, TOXCENTER, TULSA, ULIDAT, USPAT2, USPATFULL, VETU, VTB

(*File contains numerically searchable property data)

Other Sources: DSL**, EINECS**, TSCA**

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DT.CA CAplus document type: Book; Conference; Dissertation; Journal; Patent; Preprint; Report

RL.P Roles from patents: ANST (Analytical study); BIOL (Biological study); CMBI (Combinatorial study); FORM (Formation, nonpreparative); MSC (Miscellaneous); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses); NORL (No role in record)

RLD.P Roles for non-specific derivatives from patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); MSC (Miscellaneous); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)

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Li

74534 REFERENCES IN FILE CA (1907 TO DATE)
5865 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
74572 REFERENCES IN FILE CAPLUS (1907 TO DATE)
5 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

L14 ANSWER 7 OF 7 REGISTRY COPYRIGHT 2004 ACS on STN

RN 6217-54-5 REGISTRY

CN 4,7,10,13,16,19-Docosahexaenoic acid, (4Z,7Z,10Z,13Z,16Z,19Z)- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN 4,7,10,13,16,19-Docosahexaenoic acid, (all-Z)- (8CI)

CN Docosahexaenoic acid (6CI)

OTHER NAMES:

CN (4Z,7Z,10Z,13Z,16Z,19Z)-4,7,10,13,16,19-Docosahexaenoic acid

CN (4Z,7Z,10Z,13Z,16Z,19Z)-Docosahexaenoic acid

CN (all-Z)-4,7,10,13,16,19-Docosahexaenoic acid

CN Δ4,7,10,13,16,19-Docosahexaenoic acid

CN 4-cis,7-cis,10-cis,13-cis,16-cis,19-cis-Docosahexaenoic acid

CN all-cis-4,7,10,13,16,19-Docosahexaenoic acid

CN all-Z-Docosahexaenoic acid

CN Cervonic acid

CN DHA

CN Doconexent

FS STEREOSEARCH

DR 25377-50-8

MF C22 H32 O2

CI COM

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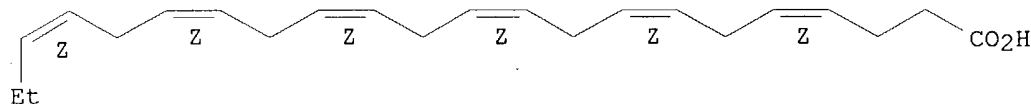
CHEMCATS, CIN, CSCHEM, EMBASE, IMSRESEARCH, MRCK*, PROMT, SYNTHLINE,
TOXCENTER, USAN, USPAT2, USPATFULL

(*File contains numerically searchable property data)

Other Sources: WHO

DT.CA Caplus document type: Conference; Dissertation; Journal; Patent
RL.P Roles from patents: ANST (Analytical study); BIOL (Biological study);
FORM (Formation, nonpreparative); MSC (Miscellaneous); OCCU
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reagent); USES (Uses)
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study); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation);
PROC (Process); RACT (Reactant or reagent); USES (Uses)
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(Reactant or reagent); USES (Uses)
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study); BIOL (Biological study); FORM (Formation, nonpreparative); OCCU
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Double bond geometry as shown.

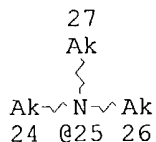
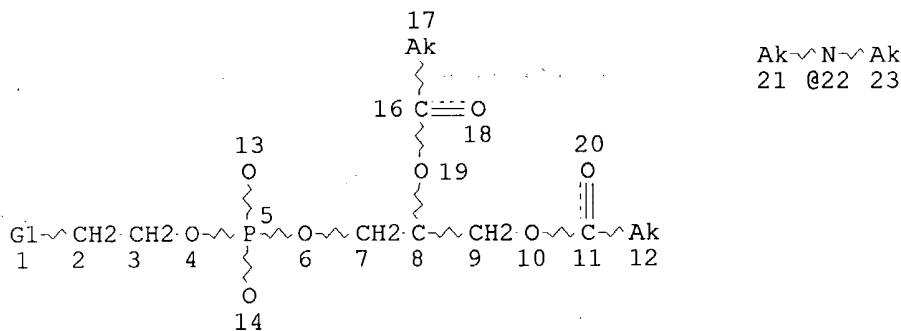


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9 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

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 L5 10 SEA FILE=REGISTRY ABB=ON PLU=ON L4 NOT IDS/CI
 L11 STR



VAR G1=22/25

NODE ATTRIBUTES:

CONNECT IS E1 RC AT 12
 CONNECT IS E1 RC AT 13
 CONNECT IS E1 RC AT 14
 CONNECT IS E1 RC AT 17
 CONNECT IS E1 RC AT 21
 CONNECT IS E3 RC AT 22
 CONNECT IS E1 RC AT 23
 CONNECT IS E1 RC AT 24
 CONNECT IS E4 RC AT 25
 CONNECT IS E1 RC AT 26
 CONNECT IS E1 RC AT 27
 DEFAULT MLEVEL IS ATOM
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 ECOUNT IS M19-X21 C AT 17

GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED
 NUMBER OF NODES IS 26

STEREO ATTRIBUTES: NONE

L12 319 SEA FILE=REGISTRY SSS FUL L11
 L13 152 SEA FILE=REGISTRY ABB=ON PLU=ON L12/COM
 L15 2068 SEA FILE=HCAPLUS ABB=ON PLU=ON "MENTAL DISORDER (L) BIPOLAR
 DISORDER"+OLD/CT
 L16 159 SEA FILE=HCAPLUS ABB=ON PLU=ON (L5 OR L13) (L) (BAC OR DMA OR
 PAC OR PKT OR THU)/RL

L17 2 SEA FILE=HCAPLUS ABB=ON PLU=ON L15 AND L16
 L18 1 SEA FILE=HCAPLUS ABB=ON PLU=ON L17 AND STOLL?/AU
 L19 32657 SEA FILE=HCAPLUS ABB=ON PLU=ON BIPOL?
 L20 4 SEA FILE=HCAPLUS ABB=ON PLU=ON (L5 OR L13) AND L19
 L21 4 SEA FILE=HCAPLUS ABB=ON PLU=ON L18 OR L20

=> d l21 ibib abs hitind hitstr 1-4

L21 ANSWER 1 OF 4 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:327204 HCAPLUS

DOCUMENT NUMBER: 139:255194

TITLE: Chronic lithium and sodium valproate both decrease the concentration of myoinositol and increase the concentration of inositol monophosphates in rat brain

AUTHOR(S): O'Donnell, T.; Rotzinger, S.; Nakashima, T. T.; Hanstock, C. C.; Ulrich, M.; Silverstone, P. H.
 CORPORATE SOURCE: Department of Psychiatry, University of Alberta Hospital, Edmonton, AB, T6G 2B7, Can.

SOURCE: European Neuropsychopharmacology (2003), 13(3), 199-207

CODEN: EURNB8; ISSN: 0924-977X

PUBLISHER: Elsevier Science B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB One of the mechanisms underlying lithium's efficacy as a mood stabilizer in **bipolar** disorder has been proposed to be via its effects on the phosphoinositol cycle (PI cycle), where it is an inhibitor of the enzyme converting inositol monophosphates to myoinositol. In contrast, sodium valproate, another commonly used mood stabilizer, appears to have no direct effects on this enzyme and was thus believed to have a different mechanism of action. In the present study, high-resolution NMR spectroscopy was used to study the chronic effects of both lithium and sodium valproate on the concns. of myoinositol and inositol monophosphates in rat brain. As predicted, lithium-treated rats exhibited a significant increase in the concentration of inositol monophosphates and a significant decrease in myoinositol concentration compared to saline-treated controls. However, unexpectedly, sodium valproate administration produced exactly the same results as lithium administration. These novel findings suggest that both lithium and sodium valproate may share a common mechanism of action in the treatment of **bipolar** disorder via actions on the PI cycle.

CC 1-11 (Pharmacology)

ST lithium sodium valproate myoinositol inositol monophosphate brain **bipolar** disorder

IT 56-40-6, Glycine, biological studies 56-73-5, Glucose-6-phosphate 57-00-1, Creatine 67-07-2, Phosphocreatine 87-89-8, Myoinositol 107-73-3, Phosphocholine 563-24-6, Glycerophosphocholine 997-55-7 1190-00-7, Glycerophosphoethanolamine

RL: BSU (Biological study, unclassified); BIOL (Biological study)

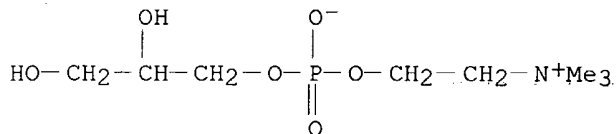
(chronic lithium and sodium valproate both decrease concentration of myoinositol and increase concentration of inositol monophosphates in rat brain)

IT 563-24-6, Glycerophosphocholine

RL: BSU (Biological study, unclassified); BIOL (Biological study)

(chronic lithium and sodium valproate both decrease concentration of myoinositol and increase concentration of inositol monophosphates in rat brain)

RN 563-24-6 HCAPLUS
 CN Ethanaminium, 2-[[(2,3-dihydroxypropoxy)hydroxyphosphinyl]oxy]-N,N,N-trimethyl-, inner salt (9CI) (CA INDEX NAME)



REFERENCE COUNT: 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 2 OF 4 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2000:719301 HCAPLUS

DOCUMENT NUMBER: 134:51298

TITLE: Chronic lithium and sodium valproate both decrease the concentration of myo-inositol and increase the concentration of inositol monophosphates in rat brain

AUTHOR(S): O'Donnell, T.; Rotzinger, S.; Nakashima, T. T.; Hanstock, C. C.; Ulrich, M.; Silverstone, P. H.

CORPORATE SOURCE: Department of Psychiatry, University of Alberta, Edmonton, AB, T6G 2B7, Can.

SOURCE: Brain Research (2000), 880(1,2), 84-91

CODEN: BRREAP; ISSN: 0006-8993

PUBLISHER: Elsevier Science B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB One of the mechanisms underlying lithium's efficacy as a mood stabilizer in **bipolar** disorder has been proposed to be via its effects on the phosphoinositol cycle (PI-cycle), where it is an inhibitor of the enzyme converting inositol monophosphates to myo-inositol. In contrast, sodium valproate, another commonly used mood stabilizer, appears to have no direct effects on this enzyme and was thus believed to have a different mechanism of action. In the present study, high resolution NMR spectroscopy was used to study the chronic effects of both lithium and sodium valproate on the concns. of myo-inositol and inositol monophosphates in rat brain. As predicted, lithium-treated rats exhibited a significant increase in the concentration of inositol monophosphates and a significant decrease in myo-inositol concentration compared to saline-treated controls. However, unexpectedly, sodium valproate administration produced exactly the same results as lithium administration. These novel findings suggest that both lithium and sodium valproate may share a common mechanism of action in the treatment of **bipolar** disorder via actions on the PI-cycle.

CC 1-11 (Pharmacology)

ST lithium valproate mental disease mechanism; brain **bipolar** disorder lithium valproate; myo inositol lithium valproate **bipolar** disorder

IT Mental disorder

(manic **bipolar** disorder; chronic lithium and sodium valproate decrease concentration of myo-inositol and increase concentration of inositol monophosphates)

IT 56-40-6, Glycine, biological studies 56-73-5, Glucose-6-phosphate 57-00-1, Creatine 67-07-2, Phosphocreatine 87-89-8, myo-Inositol

107-73-3, Phosphocholine **563-24-6**, Glycerophosphocholine
 997-55-7 1190-00-7, Glycerophosphoethanolamine 105182-27-2, Inositol
 monophosphate

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
 (Biological study); PROC (Process)

(chronic lithium and sodium valproate decrease concentration of myo-inositol
 and increase concentration of inositol monophosphates)

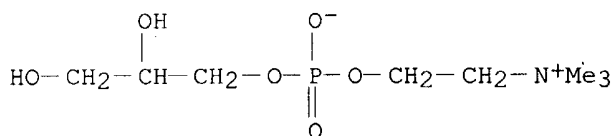
IT **563-24-6**, Glycerophosphocholine

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
 (Biological study); PROC (Process)

(chronic lithium and sodium valproate decrease concentration of myo-inositol
 and increase concentration of inositol monophosphates)

RN 563-24-6 HCAPLUS

CN Ethanaminium, 2-[[(2,3-dihydroxypropoxy)hydroxyphosphinyl]oxy]-N,N,N-
 trimethyl-, inner salt (9CI) (CA INDEX NAME)



REFERENCE COUNT: 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 3 OF 4 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2000:98343 HCAPLUS

DOCUMENT NUMBER: 132:132349

TITLE: Methods using uridine or a uridine source for
 increasing cytidine levels in vivo and treating
 cytidine-dependent human neurological diseases

INVENTOR(S): Watkins, Carol; Wurtman, Richard J.

PATENT ASSIGNEE(S): Massachusetts Institute of Technology, USA

SOURCE: PCT Int. Appl., 22 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

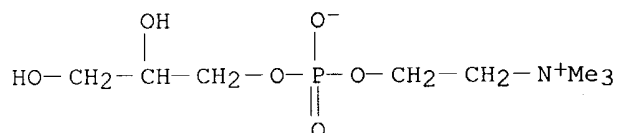
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000006174	A1	20000210	WO 1999-US17235	19990730
W: CA, JP				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2339008	AA	20000210	CA 1999-2339008	19990730
EP 1140104	A1	20011010	EP 1999-937631	19990730
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
US 2002028787	A1	20020307	US 1999-363748	19990730
JP 2003517437	T2	20030527	JP 2000-562028	19990730
PRIORITY APPLN. INFO.: US 1998-95002P P 19980731				
WO 1999-US17235 W 19990730				

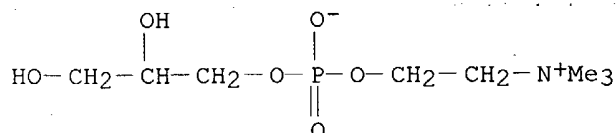
AB Methods of treating certain neurol. diseases using exogenous uridine or a

uridine source alone as a precursor of endogenous cytidine, particularly in the human brain, are disclosed. Methods are also disclosed in which exogenous uridine or a uridine source is combined either with drugs increasing uridine availability or with compds. that serve as a source of choline in phospholipid synthesis.

- IC ICM A61K031-55
ICS A61K031-70; A61K031-235; A61K031-515; A61K031-685
- CC 1-11 (Pharmacology)
- IT Mental disorder
(manic **bipolar** disorder; uridine or uridine source for increasing cytidine levels in vivo and treating cytidine-dependent human neurol. diseases)
- IT 54-03-5, Hexobendine 62-49-7, Choline 67-48-1, Choline chloride 87-67-2, Choline bitartrate, biological studies **563-24-6**, Glycerophosphatidylcholine **563-24-6D**, Glycerophosphocholine, acyl derivs. 987-78-0, CDP-choline 5909-45-5D, derivs. 5909-45-5D, derivs. 5983-09-5, 2',3'-Dideoxyuridine 23464-76-8, Choline stearate 26287-69-4, L-Uridine 35898-87-4, Dilazep 153547-98-9
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(uridine or uridine source for increasing cytidine levels in vivo and treating cytidine-dependent human neurol. diseases)
- IT **563-24-6**, Glycerophosphatidylcholine **563-24-6D**, Glycerophosphocholine, acyl derivs.
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(uridine or uridine source for increasing cytidine levels in vivo and treating cytidine-dependent human neurol. diseases)
- RN 563-24-6 HCAPLUS
- CN Ethanaminium, 2-[[[(2,3-dihydroxypropoxy)hydroxyphosphinyl]oxy]-N,N,N-trimethyl-, inner salt (9CI) (CA INDEX NAME)



- RN 563-24-6 HCAPLUS
- CN Ethanaminium, 2-[[[(2,3-dihydroxypropoxy)hydroxyphosphinyl]oxy]-N,N,N-trimethyl-, inner salt (9CI) (CA INDEX NAME)



REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 4 OF 4 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1997:717821 HCAPLUS

DOCUMENT NUMBER: 128:7311

TITLE: Fatty acids and phosphatidylcholines in the treatment of **bipolar** disorder

INVENTOR(S): Stoll, Andrew L.; Severus, Wolfram E.

PATENT ASSIGNEE(S): Brigham and Women's Hospital, USA; Stoll, Andrew L.; Severus, Wolfram E.

SOURCE: PCT Int. Appl., 13 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9739759	A2	19971030	WO 1997-US6712	19970423
WO 9739759	A3	19980115		
W: AU, CA, JP, US				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9727384	A1	19971112	AU 1997-27384	19970423
US 6344482	B1	20020205	US 1999-269361	19990322
US 2002091103	A1	20020711	US 2002-68035	20020205
US 2003012827	A1	20030116	US 2002-83913	20020227

PRIORITY APPLN. INFO.:

US 1996-16140P	P	19960424
WO 1997-US6712	W	19970423
US 1999-269361	A1	19990322

AB The present invention is directed to a method of treating patients with **bipolar** disorder by administering ω -3 fatty acids. These may be administered in a substantially purified form, as part of a pharmaceutical composition, or as part of a larger mol., e.g. a triacylglycerol, which releases free fatty acid after ingestion by a patient. The present invention is also directed to triacylglycerols which are esterified at the γ -carbon of glycerol with phosphocholine and at either the α - or β -carbon of glycerol with an ω -3 fatty acid. These ω -3 phosphatidylcholines are also used in the treatment of patients with **bipolar** disorder.

IC ICM A61K033-14

ICS A61K031-66; A61K031-20

CC 63-6 (Pharmaceuticals)

Section cross-reference(s): 1

ST polyunsatd fatty acid phosphatidylcholine **bipolar** disorderIT **Mental disorder**

(**manic bipolar disorder**; ω -3 fatty acids and phosphatidylcholines for treatment of **bipolar disorder**)

IT Drug delivery systems

(oral; ω -3 fatty acids and phosphatidylcholines for treatment of **bipolar** disorder)

IT Fatty acids, biological studies

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(polyunsatd., n-3; ω -3 fatty acids and phosphatidylcholines for treatment of **bipolar** disorder)

IT Phosphatidylcholines, biological studies

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(ω -3 fatty acids and phosphatidylcholines for treatment of **bipolar** disorder)

IT 7439-93-2D, Lithium, compds., biological studies

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(as addnl. agent; ω -3 fatty acids and phosphatidylcholines for treatment of **bipolar** disorder)

IT 6217-54-5, Docosahexaenoic acid 10417-94-4, Eicosapentaenoic acid

87879-23-0 87879-27-4 98819-78-4

198779-10-1

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(ω -3 fatty acids and phosphatidylcholines for treatment of **bipolar** disorder)

IT 87879-23-0 87879-27-4 98819-78-4

198779-10-1

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

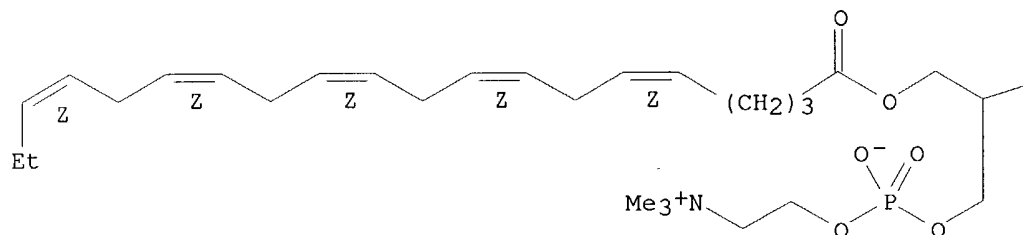
(ω -3 fatty acids and phosphatidylcholines for treatment of **bipolar** disorder)

RN 87879-23-0 HCAPLUS

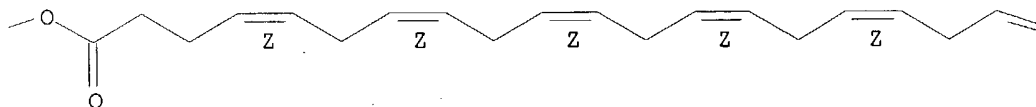
CN 3,5,8-Trioxa-4-phosphatriaconta-12,15,18,21,24,27-hexaen-1-aminium, 4-hydroxy-N,N,N-trimethyl-9-oxo-7-[[[(5Z,8Z,11Z,14Z,17Z)-1-oxo-5,8,11,14,17-eicosapentaenyl]oxy]methyl]-, inner salt, 4-oxide, (12Z,15Z,18Z,21Z,24Z,27Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A



PAGE 1-B



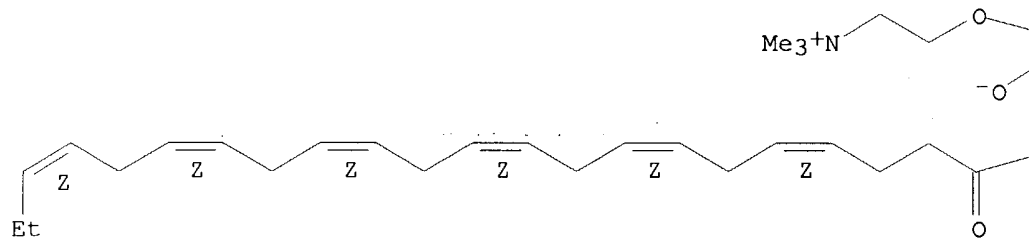
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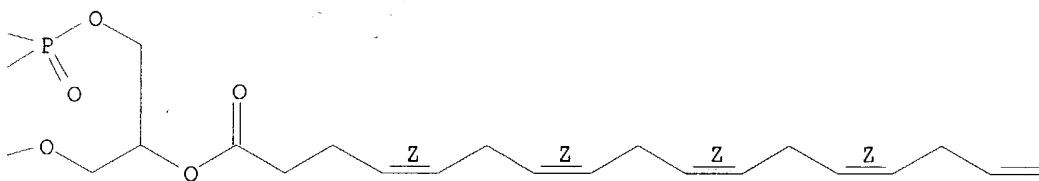
RN 87879-27-4 HCAPLUS
 CN 3,5,9-Trioxa-4-phosphahentriaconta-13,16,19,22,25,28-hexaen-1-aminium,
 4-hydroxy-N,N,N-trimethyl-10-oxo-7-[[(4Z,7Z,10Z,13Z,16Z,19Z)-1-oxo-
 4,7,10,13,16,19-docosahexaenyl]oxy]-, inner salt, 4-oxide,
 (13Z,16Z,19Z,22Z,25Z,28Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

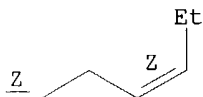
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PAGE 1-B



PAGE 1-C

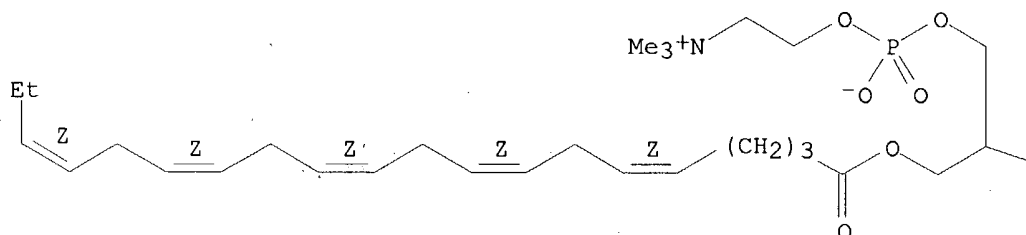


RN 98819-78-4 HCAPLUS
 CN 3,5,9-Trioxa-4-phosphanonacosa-14,17,20,23,26-pentaen-1-aminium,

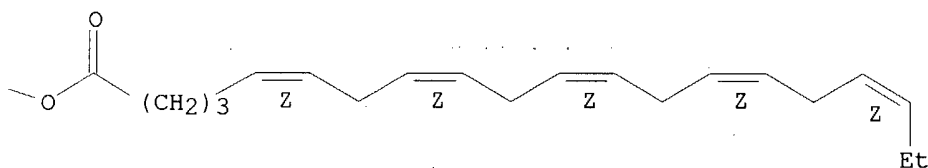
4-hydroxy-N,N,N-trimethyl-10-oxo-7-[[(5Z,8Z,11Z,14Z,17Z)-1-oxo-5,8,11,14,17-eicosapentaenyl]oxy]-, inner salt, 4-oxide, (14Z,17Z,20Z,23Z,26Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A



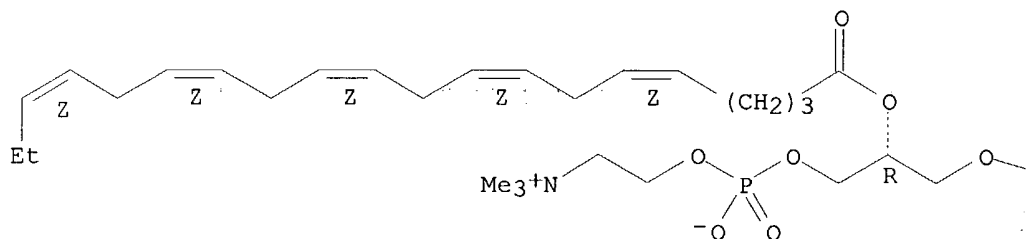
PAGE 1-B



RN 198779-10-1 HCAPLUS
 CN 3,5,9-Trioxa-4-phosphahentriaconta-13,16,19,22,25,28-hexaen-1-aminium, 4-hydroxy-N,N,N-trimethyl-10-oxo-7-[(1-oxo-5,8,11,14,17-eicosapentaenyl)oxy]-, inner salt, 4-oxide, [R-(all-Z)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
 Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

